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(54) Title: ELECTRO–OSMOTIC PUMPING SYSTEM AND METHOD

(57) Abstract

An electro–osmotic flow system and method. The system includes a capillary tube having a resistive material layer on the interior surface of the tube. The resistive material layer is coupled to a voltage source to produce a potential drop across the layer. The resistive layer is in contact with a buffer fluid injected into the tube and provides a continuous potential drop which ensures uninterrupted electro–osmotic flow of the fluid in the capillary tube.

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TITLE: ELECTRO-OSMOTIC PUMPING SYSTEM AND METHOD

FIELD OF THE INVENTION

The present invention relates to capillary electrophoresis and more particularly to an electro-osmotic flow pumping system and method.

BACKGROUND OF THE INVENTION

Electro-osmotic flow was first observed in capillary electrophoresis work. What was noticed was that in addition to the solutes, the buffer solution was moving when the electric field was applied. Not only was the buffer solution moving, but also its velocity profile was practically flat, leading to the term 'plug' flow.

Capillary electrophoresis is generally used for fluid material separations. The electrophoretic effect is a competition between the electric field force on an ionized chemical group in solution and the viscous drag of that group as it moves the solution, also known as the buffer. The electro-osmotic flow was observed to carry the entire buffer fluid along the capillary as the electrophoresis was occurring.

Electro-osmotic flow depends critically on the interaction between the interior surface of the capillary tube and the buffer solution. When the buffer fluid is placed in the capillary tube, the inner surface takes on a negative charge. The origin of this charge is not adequately understood. It may be due to the ionization of the tube itself, or absorption of buffer ions. Even Teflon tubes will exhibit electro-osmotic flow.

The choice for most capillary electrophoresis applications is a fused silica capillary tube 1 as depicted in Fig. 1. Referring to Fig. 1, surface silanol groups (Si-OH) are ionized into negatively charged silanoate groups ($Si-O^-$) 2 at pH levels above 3. This results in the interior surface 2 of the capillary tube becoming negatively charged and attracting some positive buffer ions from the solution. The positive buffer ions become practically bound to the interior surface 2 of capillary tube 1 and result in a bound cationic layer (indicated generally by reference 5). The bound cationic layer 5 is not sufficient to neutralize the electric field at the interior surface 2 of the capillary tube wall, and a second mobile cationic layer 6 of positive buffer ions is drawn towards the interior surface of the capillary tube 1, forming a complete cationic diffuse double layer indicated by reference 7 in Fig. 1(b).

When an electric field is applied, the mobile cationic layer 6 moves while the inner bound cationic layer 5 remains stationary. Since the cations in the mobile cationic layer 6 are solvated, the buffer fluid is dragged along by the cations in the mobile cationic layer 6. Between the bound cationic layer 5 and the mobile cationic layer 6, there is a plane of shear 8. An electrical imbalance is created at the plane of shear 8 which is the potential difference across the cationic layers 5 and 6. The potential difference is commonly referred to as the "Zeta potential".

Practical electro-osmotic flow systems suffer from the problem of bubble formation in the capillary tube. As depicted in Fig. 2, if a bubble 12 enters the capillary tube 1 and is able to completely span the capillary tube 1,

then the buffer fluid 11 is divided into two separate buffer fluid segments denoted by references 11a and 11b. The separation of the buffer fluid 11 into the segments 11a and 11b causes the ionic current flow due to the mobile layer 6 to be interrupted and as a result the flow of the buffer fluid 11 is halted. Thus, a bubble 12 in the capillary tube 1 can cause an electro-osmotic flow apparatus to completely fail.

Two principle approaches have been taken in the art to enhance electro-osmotic flow in a capillary tube. The first involves chemical modification, and the second involves electrical modification.

Nearly all of the known chemical-based techniques focus on the modification of the diffuse double layer 7 (Fig.1(b)) required to produce electro-osmotic flow. Capillary tubes made of fused silica (as discussed above) can have their inner surfaces treated chemically to increase the natural formation of bound, ionized surface groups. One such technique involves pre-treating the capillary tube with NaOH.

Another known technique involves adding chemicals that block the formation of the bound surface ions 5 and thereby work to decrease the "Zeta potential". One such technique involves covalent bonding of monomolecular layers of polyacrylamide to the inner surface of the capillary tube in order to minimize both electro-osmotic flow and buffer absorption. This technique works by chemically shielding the bound charges already on the inner surface of the capillary tube thereby reducing the Zeta potential, and so the electro-osmotic flow.

Nevertheless, none of these known chemical modification procedures is able to overcome the problem of bubble formation and its interruption of the net ionic current flow within the capillary tube.

Electrical modification is another known technique for enhancing electro-osmotic flow in capillary tubes. One electrical modification technique involves utilizing conventional solid semiconductor materials in the micro-fabrication of the capillary tubes. The semiconductor construction of capillary tubes provides the ability to control voltages along the inner surface of the capillary tube and thereby the Zeta potential. However, known solid semiconductor materials, such as silicon, have been found to be ill-suited to electro-osmotic flow systems because the breakdown electric fields are often much lower than the fields required for producing the electro-osmotic flow. For example, to be useable in a practical electro-osmotic application, a solid semi-conductor construction (for example, silicon) would need to support a voltage potential of 1000V. It will be understood that this is far above the breakdown voltage defined by silicon resistive layers, i.e. formed by oxidation on the inner surface of the capillary tube. Therefore, the use of solid semiconductor constructions in capillary devices also requires the use of insulating coatings which ultimately complicate the micro-fabrication of these devices.

Another known approach using electrical modification involves the application of 'radial' electric fields to the capillary tube. As shown in Fig. 3, a capillary tube 20 (made of a standard insulating material) is covered by a conducting sheath 21 having a very high resistance value. The sheath 21 is coupled to a power

supply 22 and charged to some specified voltage. Since the sheath 21 has a very poor conductivity, the Joule heating effect is minimal. The capillary tube 20 and the sheath 21 effectively form a large cylindrical capacitor. The accumulation of charge on the inner surface of the sheath 21 alters the radial electric field inside the capillary tube 20 and thereby affects the Zeta potential. In this way the electro-osmotic flow may be continuously controlled by a continuous adjustment of the voltage applied to the sheath 21.

Again, neither of these known electrical modification techniques is capable of dealing with the problem of bubble formation within the capillary tube. Accordingly, there remains a need for a solution to the problem of bubble formation in a capillary tube in electro-osmotic applications.

BRIEF SUMMARY OF THE INVENTION

The present invention provides an apparatus and method for electro-osmotic flow in a capillary tube.

In a first aspect, the present invention provides a capillary tube for use in an electro-osmotic flow system, the capillary tube comprises, (a) a cylindrical tube having an interior wall and an exterior wall; (b) a resistive material layer, the resistive material layer is affixed to the interior wall; (c) the resistive material layer includes a pair of terminal ends for coupling to a power source to produce a potential drop across the resistive material layer.

In a second aspect, the present invention provides an electro-osmotic flow control system for

controlling the flow of one or more buffer fluids, the electro-osmotic flow control system comprises: (a) a capillary tube having an interior wall and an exterior wall, and an input end and an output end, the input end provides an input port for receiving the buffer fluids, and the output end provides an output port for egress of the buffer fluids; (b) the capillary tube includes a resistive material layer, the resistive material layer is affixed to the interior wall; (c) a power source coupled to the resistive material layer for producing a potential drop across the resistive material layer.

In another aspect, the present invention provides a method for producing an electro-osmotic flow in a capillary tube, the capillary tube comprises a cylindrical tube having an interior wall and an exterior wall, and includes a resistive material layer affixed to the interior wall, the method comprises the steps of: (a) injecting a buffer fluid into one end of the capillary tube; (b) applying an external voltage to the resistive material layer to produce a potential drop across the layer; and (c) controlling the potential drop to vary the Zeta potential and control the electro-osmotic flow of the buffer fluid in the capillary tube.

In yet another aspect, the present invention provides, an electro-osmotic flow system for controlling the flow of a plurality of buffer fluids, the electro-osmotic flow control system comprises: (a) an input capillary tube having an interior wall and the interior wall includes a resistive material layer, and the input capillary tube has an input and an output port, the input provides an input port for receiving the buffer fluids; (b) a first branch capillary tube having an interior wall and

the interior wall includes a resistive material layer, and the first branch capillary tube has an input and an output, the input is coupled to the output port on the input capillary tube; (c) a second branch capillary tube having an interior wall and the interior wall includes a resistive material layer, and the second branch capillary tube has an input and an output, the input being coupled to the output port on the input capillary tube; (d) a voltage source having a plurality of voltage outputs, one voltage output is coupled to the input capillary tube for producing a potential drop across the resistive material in response to a control signal, a second voltage output is coupled to the first branch capillary tube for producing a potential drop across the resistive material in response to a control signal, and a third voltage output os coupled to the second branch capillary tube for producing a potential drop across the resistive material in response to a control signal; and (e) a controller for controlling the voltage source, the controller includes an output control port coupled to the voltage source for outputting the control signals to control the potential drop in each of the capillary tubes wherein the potential drop controls the flow of the buffer fluid in the associated capillary tube.

BRIEF DESCRIPTION OF THE DRAWINGS

Reference will now be made to the accompanying drawings, which show by way of example, a preferred embodiment of the present invention, and in which:

Fig. 1(a) shows a conventional capillary tube according to the prior art;

Fig. 1(b) shows the formation of a diffuse double layer in the capillary tube of Fig. 1(a);

Fig. 2 shows the capillary tube of Fig. 1(a) with a bubble formed inside the tube;

Fig. 3 shows the capillary tube of Fig. 1(a) with an arrangement for producing a radial electric field according to the prior art;

Fig. 4(a) is a cross-sectional view of an electro-osmotic flow system according to the present invention;

Fig. 4(b) is an end view of the electro-osmotic flow system of Fig. 4(a);

Fig. 5 shows the capillary tube of Fig. 4 with a bubble formed inside the tube;

Fig. 6 shows the capillary tube of Fig. 4 with two bubbles formed inside the tube according to a method for separating fluid segments; and

Fig. 7 shows a network of capillary channels for controlling the flow of a plurality of fluid segments according to another aspect of the invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Reference is made to Figs. 4(a) and 4(b), which show an electro-osmotic flow system 100 according to the present invention.

As shown in Fig. 4, the electro-osmotic flow system 100 according to the invention comprises a capillary tube 101 having an inner surface or wall 102. The inner surface 102 is coated with a resistive material 104. As

shown in Fig. 4, the resistive material 104 is not sealed or otherwise altered, and resides in direct contact with the buffer fluid 99. A power supply 106 is connected to the resistive material layer 104 and a voltage is applied directly to the resistive layer 104. Application of the voltage (e.g. in the range of 1 KV) to the resistive material layer 104 results in a continuous electric potential drop that is experienced by the buffer fluid 99 at all points in the capillary tube 101.

The resistive material preferably comprises a highly resistive material, for example, a semiconducting polymer, such as polyaniline, polypyrrole, or the like. The resistances of these polymers can be adjusted over a very large range to suit the particular application. It has been found that a resistance in the range of approximately 100 MegaOhms to 1000 MegaOhms is suitable for most applications, and for some applications the resistance value will be dependent on the geometry of the layer 104 and/or the interior channel of the capillary tube 101. In addition to the semiconducting polymers described above, a gel for ion exchange or an ion exchange polymer such as PVP (polyvinylpyrrolidone) or even ordinary agar gel is also suitable. Unlike conventional solid semiconductor materials (i.e. silicon), a semiconducting polymer does not form an oxidation layer and is thereby able to conduct the electric current across its thickness.

As shown in Fig. 4(b), coating the inner surface of the capillary tube 101 with the resistive material 104 provides an electric current (ionic) conductive path at every point in the capillary tube 101 regardless of local conditions. If the flow of the buffer fluid 99 is interrupted by the formation of a bubble 120, i.e.

resulting in two buffer fluid segments 99a and 99b, then both fluid segments 99a and 99b on either side of the bubble 120 continue to experience the electric force through contact with the energized resistive layer 104 and so will therefore continue to move in direction of arrow 121, pushing the bubble 120 along with the fluid 99. This is because the ionic current flow can continue through the conductive path provided by the resistive layer 104 coating the inner surface 102 of the capillary tube 101.

Reference is next made to Fig. 6, which shows another aspect of the electro-osmotic flow system 100 according to the present invention. According to this aspect, one or more bubbles 122 are utilized as separators to separate different fluid segments and control their translation through the capillary tube 101. The bubble 122 separates a first buffer fluid segment 98a from a second buffer fluid segment 98b. Each buffer fluid segment 98 may comprise the same buffer fluid, or a different set of materials, or chemical reactions. The bubble separator 122 provides an effective barrier between the fluid segments 98a and 98b, and the fluid segments 98a and 98b can be translated or moved through the capillary tube 101 by energizing the resistive material layer 104 while at the same time using the bubble 122 to maintain the separation. The bubbles 122 may be injected when the fluid 98 is injected into the capillary tube 101 or formed after the fluid 98 is injected, for example, by injecting air into the tube 101 through a one-way valve 121 located at one end of the capillary tube 101. The width of the bubbles 122 may also be varied depending on the separation desired, characteristics of the fluids, etc.

Reference is next made to Fig. 7, which extends the mechanism of Fig. 6 to a network arrangement of capillary tubes 200 according to another aspect of the present invention. As shown in Fig. 7, the networked arrangement 200 comprises a main input capillary tube 201. The main capillary tube 201 has an input port for receiving buffer fluid segments 300. The buffer fluid segments 300 are denoted individually as 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314 and 315. Each of the fluid segments 300 may contain different materials or a different set of chemical reactions. The buffer fluid segments 300 are separated by bubble separators (as described above) and are denoted generally by reference 320. As shown in Fig. 7, the output of the main capillary tube 201 is divided into the three capillary tube branches denoted by references 204, 206 and 208, respectively. The second capillary tube 206 includes a capillary tube 214 with a different geometry. The third capillary tube 208 includes four output capillary tubes denoted by references 216, 218, 220, and 222. The capillary tube 222, in turn, is divided into two capillary channels 223a and 223b. The successive electric energizing of each of the capillary tube branches allows the buffer fluid segments 300 to be moved within the network 200. These network components allow the fluid segments 300 to be moved anywhere within the network 200 at will.

As also shown in Fig. 7, each capillary tube branch 201-223 is provided with a controllable power source or control voltage input 230, indicated individually as 230a, 230b, 230c, 230d, 230e, 230f, 230g, 230h, 230i, 230j and 230k. The controllable power sources or voltage inputs 230 are coupled to a controller 240 which energizes the respective capillary tube branches 201-223 to move the

buffer fluid segment 300 in the respective capillary tube segment 300 utilizing the electro-osmotic flow mechanism according to the invention. To move a fluid segment, for example fluid segments 301, 302 and 303, capillary tube branches 201, 204 and 210 are energized by the associated voltage input, i.e. 230a, 230b and 230c, while the remaining voltage inputs 230 are held off. Similarly, other fluid segments 300 can be moved through the network 200 under the control of the controller 240.

In summary, the electro-osmotic flow system 100 provides several advantages. First, the resistive material coating 104 on the inner surface 102 of capillary tube 101 solves the problem of bubble formation and consequent interruption of the ionic current flow. The resistive material coating 104 of the inner surface 102 of the capillary tube 101 provides both a continuous source of electromotive force and a continuous, uninterruptable current path for any number of buffer fluid segments within the capillary tube 101. According to another aspect the buffer fluid segments are separated by bubble separators. Thus, the formation of a bubble does not stop the electro-osmotic flow within the buffer fluid segment and the electric field force continues to drive that buffer fluid segment down the capillary.

WHAT IS CLAIMED IS:

1. A capillary tube for use in an electro-osmotic flow system, said capillary tube comprising:

(a) a cylindrical tube having an interior wall and an exterior wall;

(b) a resistive material layer, said resistive material layer being affixed to said interior wall; and

(c) said resistive material layer including a pair of terminal ends for coupling to a power source to produce a potential drop across said resistive material layer.

2. The capillary tube as claimed in claim 1, wherein said resistive material layer has a resistance in the range of substantially 100 MegaOhms to 1000 MegaOhms.

3. The capillary tube as claimed in claim 2, wherein said resistive material layer is formed from a semiconducting polymer selected from a group consisting of polyaniline and polypyrrole.

4. The capillary tube as claimed in claim 2, wherein said resistive material layer is formed from a material selected from a group consisting of an ion exchange gel, agar gel and an ion exchange polymer.

5. An electro-osmotic flow control system for controlling the flow of one or more buffer fluids, said electro-osmotic flow control system comprising:

(a) a capillary tube having an interior wall and an exterior wall, and an input end and an output end, said input end providing an input port for receiving the buffer fluids, and said output end providing an output port for outputting the buffer fluids;

(b) said capillary tube including a resistive material layer, said resistive material layer being affixed to said interior wall; and

(c) a power source coupled to said resistive material layer for producing a potential drop across said resistive material layer.

6. The capillary tube as claimed in claim 5, wherein said resistive material layer has a resistance in the range of substantially 100 MegaOhms to 1000 MegaOhms.

7. The capillary tube as claimed in claim 6, wherein said resistive material layer is formed from a semiconducting polymer selected from a group consisting of polyaniline and polypyrrole.

8. The capillary tube as claimed in claim 6, wherein said resistive material layer is formed from a material selected from a group consisting of an ion exchange gel, an agar gel and an ion exchange polymer.

9. The electro-osmotic flow control system as claimed in claim 4, further including a controller, said controller being coupled to a control input on said power source and including programmable control means for controlling said power source.

10. The electro-osmotic flow control system as claimed in claim 9, further including a bubble injector, said bubble injector being operatively coupled to said capillary tube for injecting a bubble into the interior of said capillary tube.

11. A method for producing an electro-osmotic flow related to a Zeta potential in a capillary tube, said capillary tube comprising a cylindrical tube having an interior wall and an exterior wall, and including a resistive material layer affixed to the interior wall, said method comprising the steps of:

(a) injecting a buffer fluid into one end of said capillary tube;

(b) applying an external voltage to said resistive material layer to produce a potential drop across said layer; and

(c) controlling said potential drop to vary the Zeta potential and control the electro-osmotic flow of the buffer fluid in said capillary tube.

12. The method as claimed in claim 11, further including the steps of injecting a bubble after injection of said buffer fluid into said capillary tube, and then injecting another buffer fluid into said capillary tube, wherein said bubble forms a separator between the two buffer fluids.

13. An electro-osmotic flow system for controlling the flow of a plurality of buffer fluids, said electro-osmotic flow control system comprising:

(a) an input capillary tube having an interior wall and said interior wall including a resistive material layer, and said input capillary tube having an input and an output port, said input providing an input port for receiving the buffer fluids;

(b) a first branch capillary tube having an interior wall and said interior wall including a resistive material layer, and said first branch capillary tube having an input

and an output, said input being coupled to the output port on said input capillary tube;

(c) a second branch capillary tube having an interior wall and said interior wall including a resistive material layer, and said second branch capillary tube having an input and an output, said input being coupled to the output port on said input capillary tube;

(d) a voltage source having a plurality of voltage outputs, one of said voltage outputs being coupled to said input capillary tube for producing a potential drop across said resistive material in response to a control signal, a second of said voltage outputs being coupled to said first branch capillary tube for producing a potential drop across said resistive material in response to a control signal, and a third of said voltage outputs being coupled to said second branch capillary tube for producing a potential drop across said resistive material in response to a control signal; and

(e) a controller for controlling said voltage source, said controller including an output control port coupled to said voltage source for outputting said control signals to control the potential drop in each of said capillary tubes wherein said potential drop controls the flow of the buffer fluid in the associated capillary tube.

14. The electro-osmotic flow system as claimed in claim 13, further including a bubble injector, said bubble injector being operatively coupled to said input capillary tube for injecting one or more bubbles into the interior of the said input capillary tube in response to a control signal, wherein said injected bubbles form separators between said buffer fluids in said capillary tubes.

15. The capillary tube as claimed in claim 14, wherein said resistive material layer has a resistance in the range of substantially 100 MegaOhms to 1000 MegaOhms.

16. The capillary tube as claimed in claim 15, wherein said resistive material layer is formed from a semiconducting polymer selected from a group consisting of polyaniline and polypyrrole.

17. The capillary tube as claimed in claim 15, wherein said resistive material layer is formed from a material selected from a group consisting of an ion exchange gel, an agar gel and an ion exchange polymer.

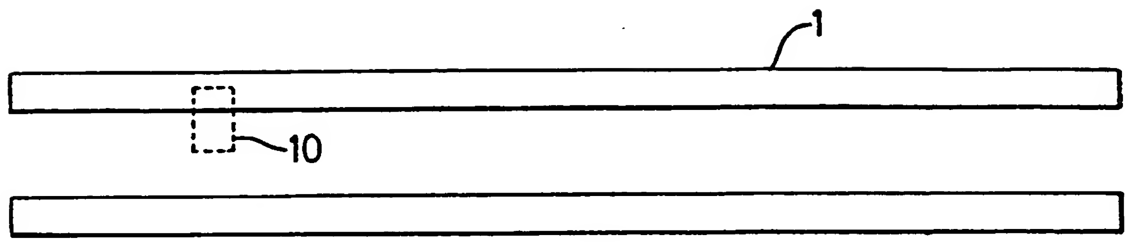


FIG. 1a
(PRIOR ART)

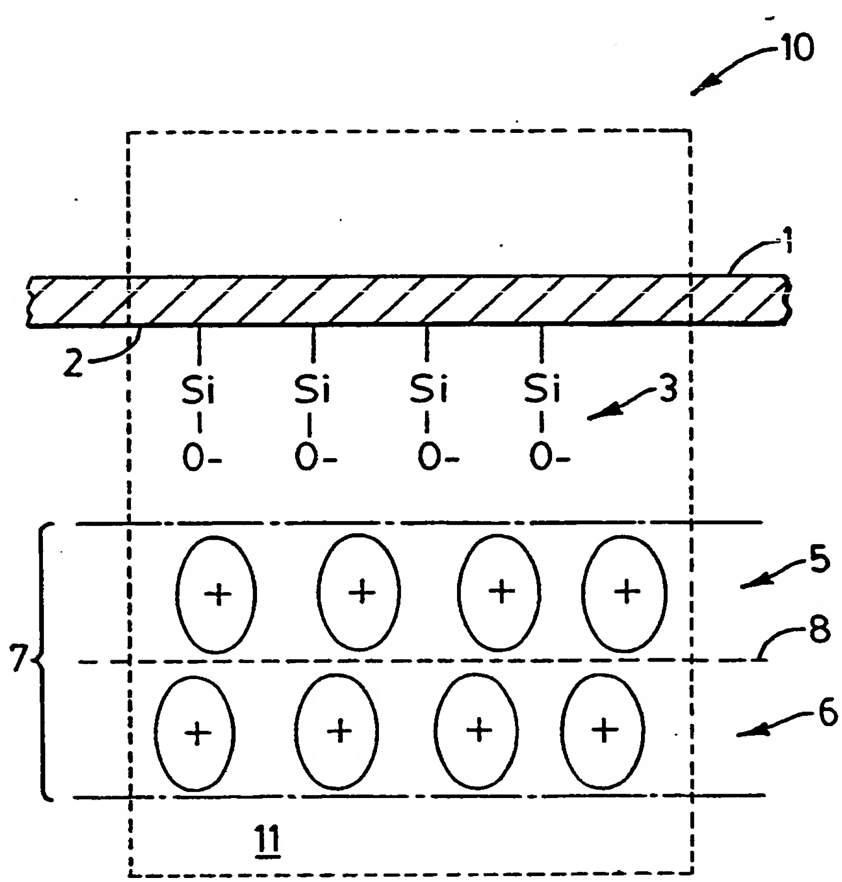


FIG. 1b
(PRIOR ART)

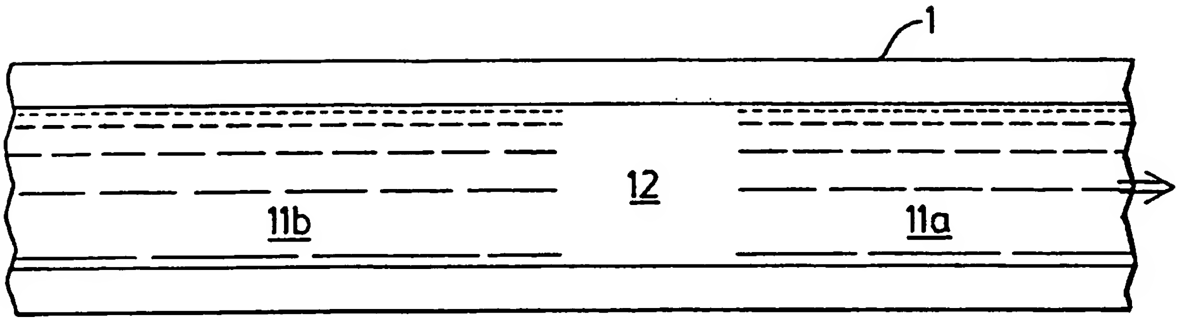


FIG. 2
(PRIOR ART)

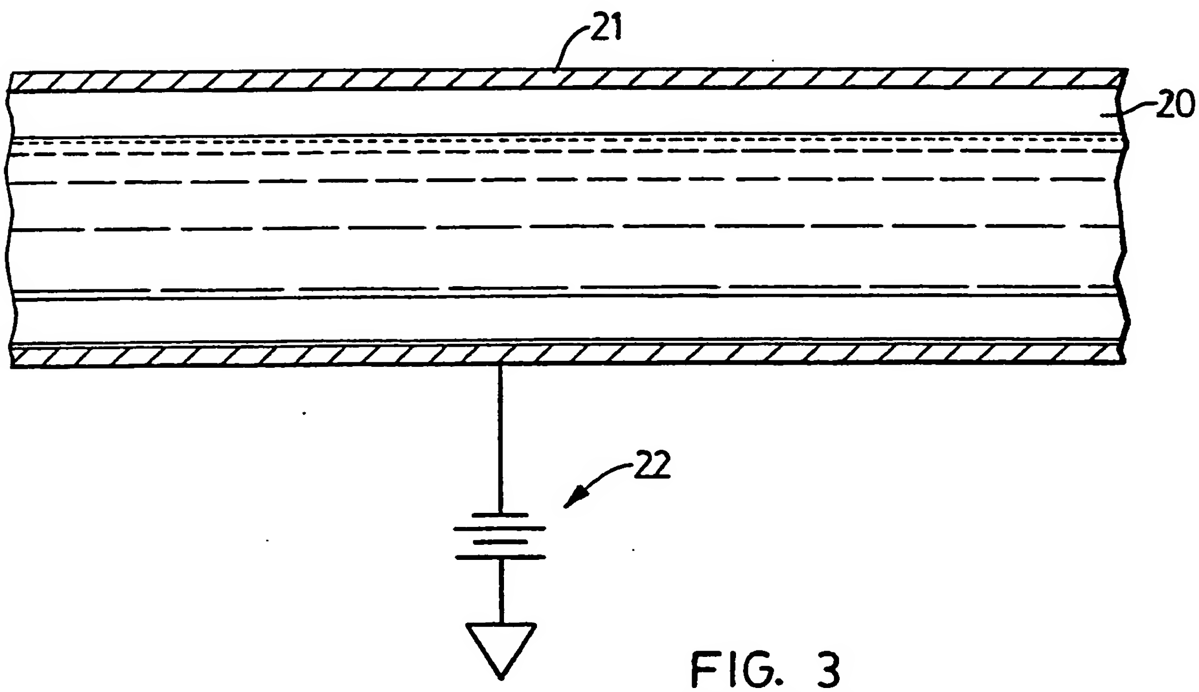


FIG. 3
(PRIOR ART)

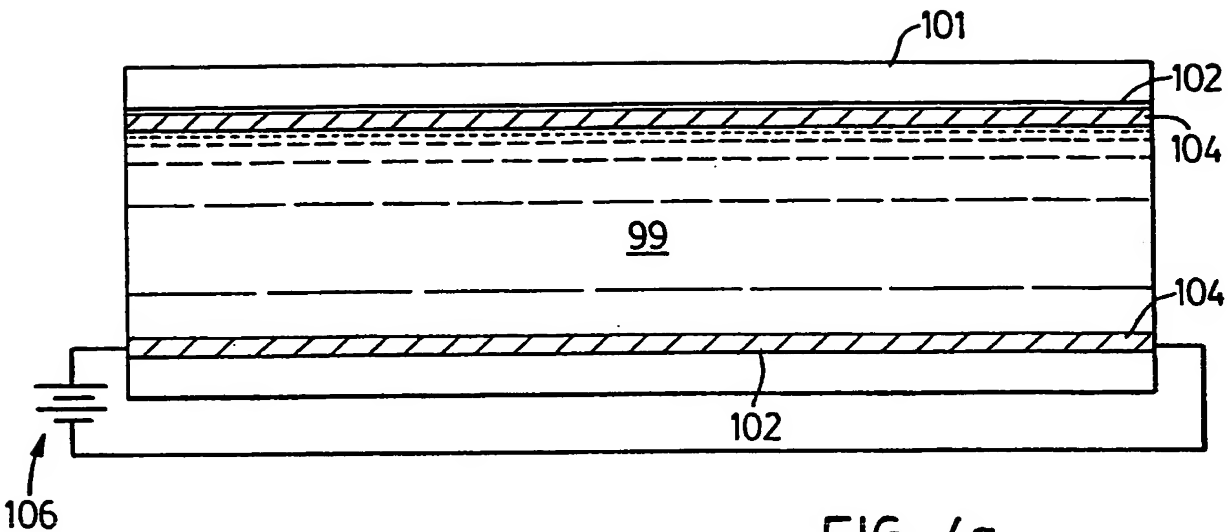


FIG. 4a

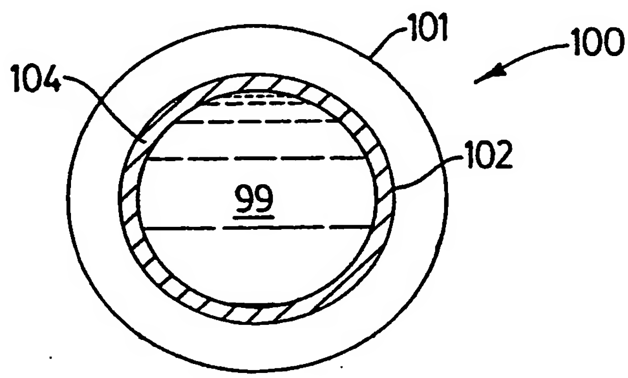


FIG. 4b

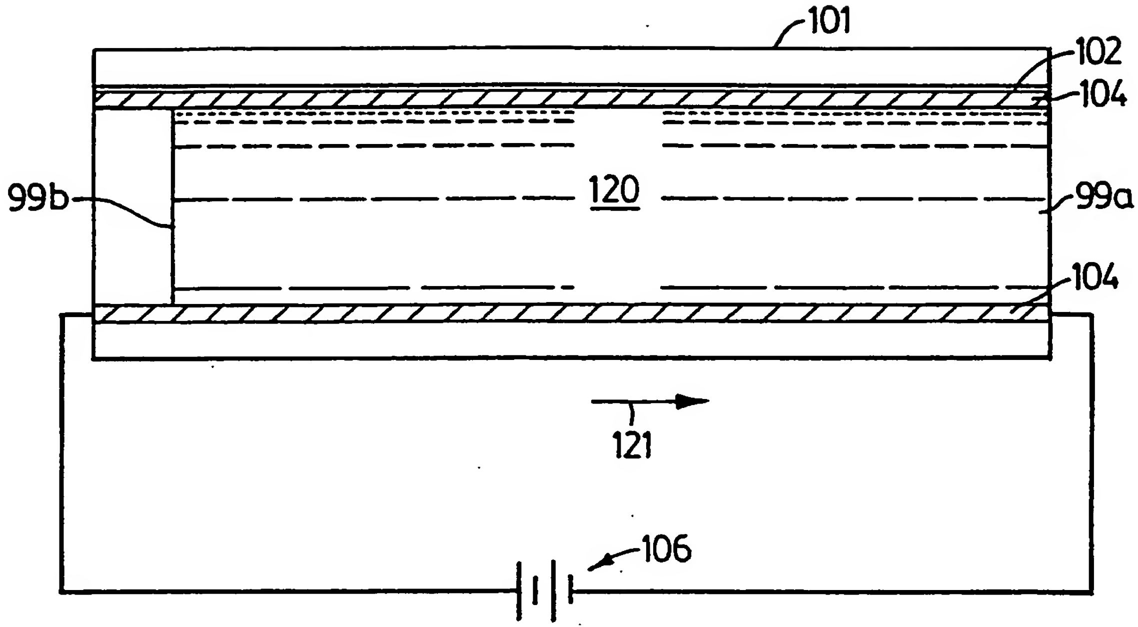
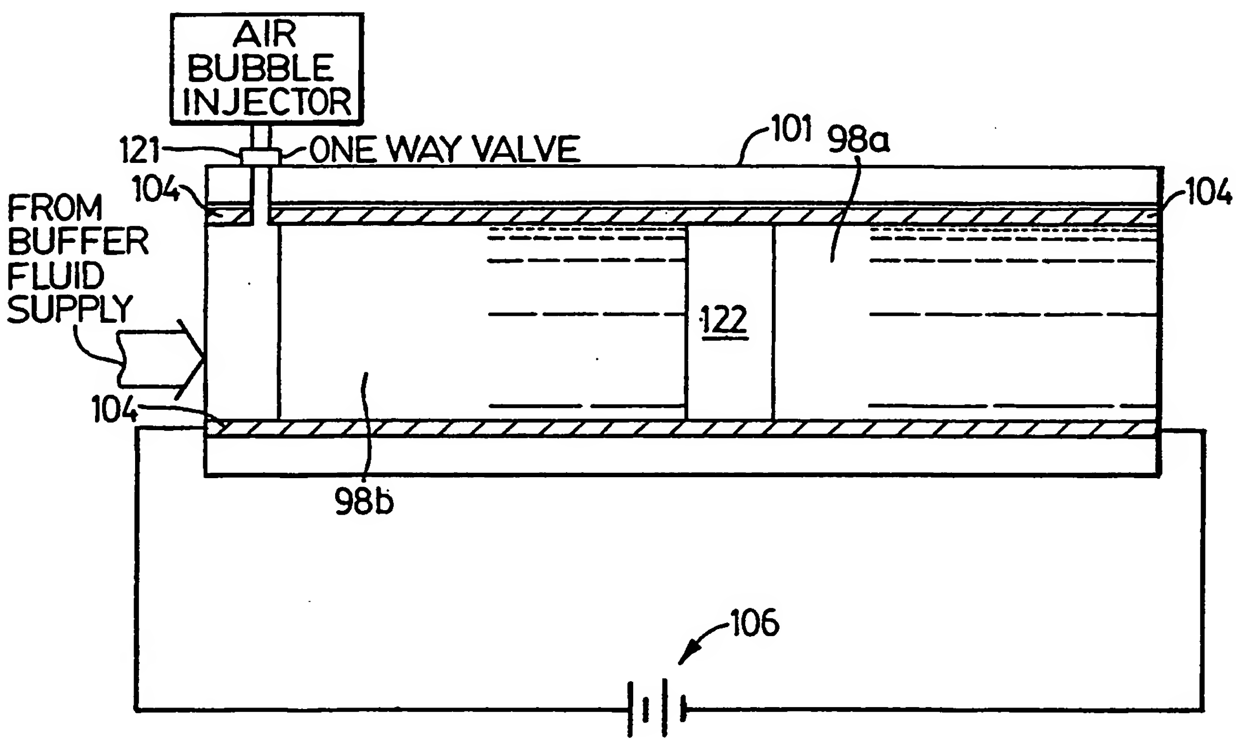

101
102
104
99b
120
99a
104
121
106

FIG. 5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FROM BUFFER FLUID SUPPLY
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98b
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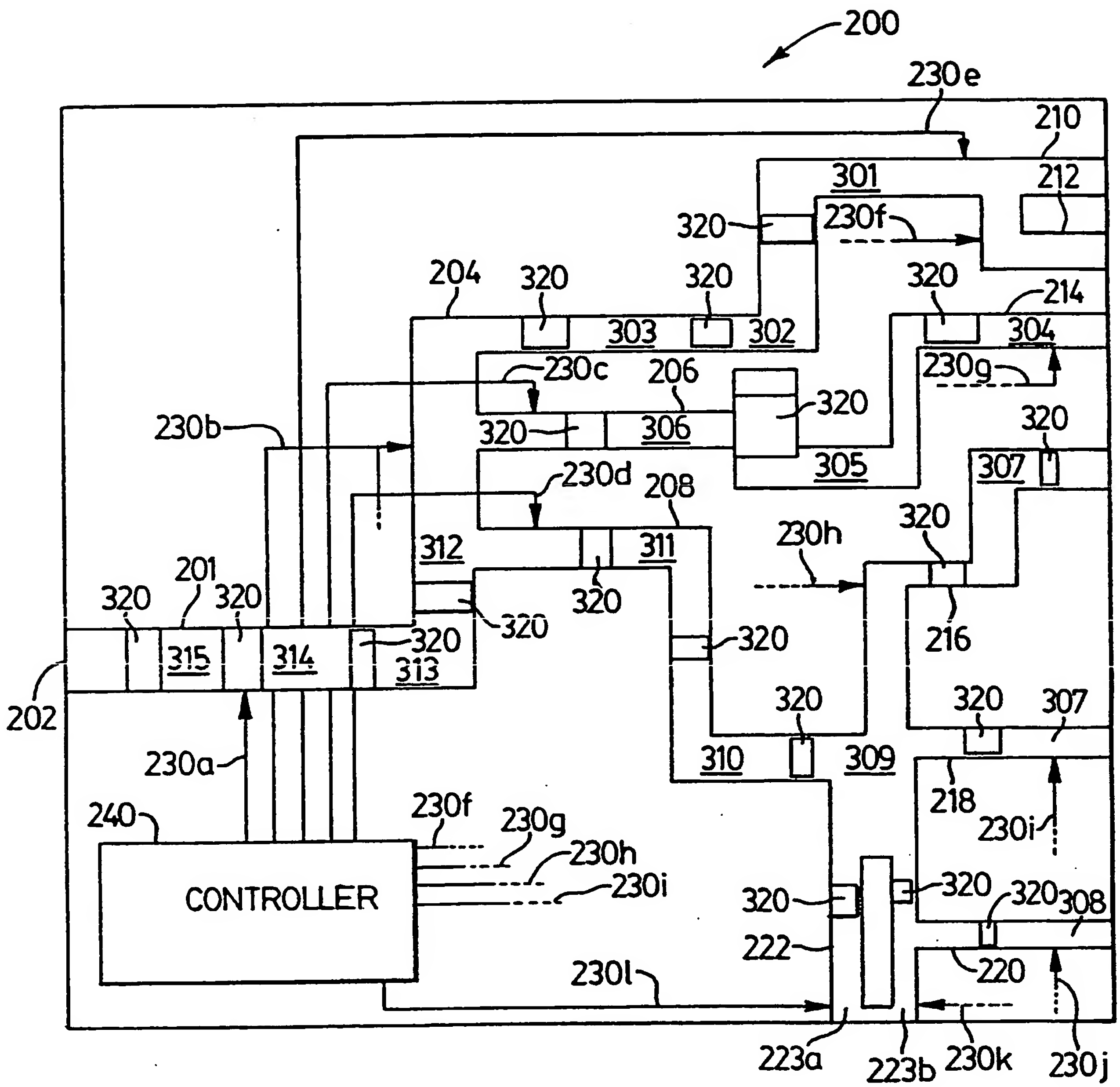
FIG. 6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230i
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222
220
230l
223a
223b
230k
230j

FIG. 7

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 00/00345

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N27/447

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N B01J B01L B01D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 639 768 A (HEWLETT PACKARD CO) 22 February 1995 (1995-02-22) abstract; claims 3,9	1,5
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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5 July 2000	18/07/2000

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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